

providing a sample potentially containing one or more target nucleotide sequences with a plurality of sequence differences;

providing a plurality of oligonucleotide probe sets, each set characterized by (a) a first oligonucleotide probe, having an oligonucleotide target-specific portion and an oligonucleotide addressable array-specific portion, wherein the oligonucleotide addressable array-specific portion is separate and distinct from the oligonucleotide target-specific portion, and (b) a second oligonucleotide probe, having a target-specific portion and a detectable reporter label, wherein the oligonucleotide probes in a particular set are suitable for ligation together when hybridized adjacent to one another on a corresponding target nucleotide sequence, but have a mismatch which interferes with such ligation when hybridized to any other nucleotide sequence present in the sample;

providing a ligase,

blending the sample, the plurality of oligonucleotide probe sets, and the ligase to form a mixture;

subjecting the mixture to one or more ligase detection reaction cycles comprising a denaturation treatment, wherein any hybridized oligonucleotides are separated from the target nucleotide sequences, and a hybridization treatment, wherein the oligonucleotide probe sets hybridize at adjacent positions in a base-specific manner to their respective target nucleotide sequences, if present in the sample, and ligate to one another to form a ligated product sequence containing (a) the addressable array-specific portion, (b) the target-specific portions connected together, and (c) the detectable reporter label, and, wherein the oligonucleotide probe sets may hybridize to nucleotide sequences in the sample other than their respective target nucleotide sequences but do not ligate together due to a presence of one or more mismatches and individually separate during the denaturation treatment;

providing a solid support with different capture oligonucleotides immobilized at particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the addressable array-specific portions;

contacting the mixture, after said subjecting, with the solid support under conditions effective to hybridize the addressable array-specific portions to the capture oligonucleotides in a base-specific manner, thereby capturing the addressable array-specific portions on the solid support at the site with the complementary capture oligonucleotide; and